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NewsScan
NIDA ADDICTION RESEARCH NEWS

NEWS UPDATE

Research News

Study Sheds New Light on Mechanism Behind Stimulant Medication for ADHD

New research involving the drug methylphenidate (Ritalin) is shedding light on how certain stimulant drugs impact the brain to improve attention and concentration for certain academic tasks. Methylphenidate is used widely to treat attention deficit hyperactivity disorder (ADHD), a neurological disorder characterized by developmentally inappropriate behavior, including poor attention skills, impulsivity, and hyperactivity. It is estimated to affect between 3 and 5 percent of the U.S. school-aged population, and also can affect adults.

In the study, the researchers, including NIDA Director Dr. Nora Volkow and scientists at Brookhaven National Laboratory, used positron emission tomography (PET) to examine brain chemistry in 16 healthy adult men and women without ADHD who were given methylphenidate or a placebo. After receiving the drug or placebo, the participants performed a series of mathematical tasks or looked at neutral images of scenery.

The PET scans showed that when participants received methylphenidate and worked through the mathematical tasks, they experienced a significant increase in extracellular dopamine. Dopamine is a brain chemical involved in pleasure/reward and motivation. These participants were also more likely to describe the mathematical tasks as interesting, exciting, and motivating.

A similar rise in extracellular dopamine levels was not seen among the participants who received the placebo and performed tasks, or those who received methylphenidate and viewed the neutral images. In addition, when the tasks were paired with placebo, participants were more likely to describe them as tiresome and boring.

- **WHAT IT MEANS:** Stimulant drugs like methylphenidate work to raise levels of extracellular dopamine, a key chemical in motivation, which can enhance interest in performing an academic task. A better understanding of this mechanism may lead to the development of other medications that have similar chemical effects in the brain, and help people with ADHD improve focus on and motivation for performing academic tasks. The study findings also support developing educational strategies that make schoolwork more interesting as a nonpharmacologic way to treat ADHD.

The study was funded by NIDA and the Department of Energy. It was published in the July 2004 issue of the *American Journal of Psychiatry*.

PET Study Highlights Mechanism Involved in Nicotine Craving

Researchers at UCLA's David Geffen School of Medicine have used positron emission tomography (PET) to reveal the mechanism through which bupropion, a smoking cessation drug, works in the brain to reduce cigarette cravings.

The scientists used PET imaging to examine brain activity in bupropion-medicated and unmedicated smokers who were exposed to smoking cues, such as the sight and feel of a cigarette. They were able to show that in the presence of bupropion, brain cells in the anterior cingulate cortex—a region known to be involved in drug craving—do not activate in response to cigarette-related cues. Until now, scientists and clinicians knew the drug reduced the urge to smoke, but the central nervous system process by which it did so was unknown.

Bupropion is marketed as Zyban for smoking cessation.

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Thirty-seven otherwise healthy smokers participated in the trial. Seventeen received bupropion for an average of 5.6 weeks; 20 were unmedicated. All participants underwent two PET scanning sessions. During the PET scans, the people either watched a smoking-oriented video and held a cigarette, or viewed a nature video and held a neutral object, like a pen. The researchers also assessed the participants' cravings for cigarettes through analysis of scores on the Urge to Smoke Scale. Bupropion-treated smokers had lower "Urge to Smoke" scores than untreated smokers. They also reported smoking fewer cigarettes per day.

- **WHAT IT MEANS:** This study increases our understanding of the basic nervous system mechanisms involved in drug craving, and how cues like smelling and seeing a cigarette can drive the impulse to smoke. A more complete understanding of these mechanisms can aid in the development of more effective treatment strategies.

The NIDA-funded study, by Dr. Arthur Brody and his colleagues, was published online in the April 2004 issue of *Psychiatry Research: Neuroimaging*.

Antiseizure Drug May Help Treat Cocaine Addiction

Results of recent research suggest that combining the antiseizure medication topiramate with one form of behavioral therapy may effectively treat cocaine addiction.

Researchers with the University of Pennsylvania School of Medicine in Philadelphia enrolled 40 people in a 13-week, placebo-controlled, double-blind study. Participants received placebo or an escalating daily dose of topiramate for 8 weeks (they initially received a dose of 25 mg daily, which was increased by 25 mg per week until the maximum dose of 200 mg per day was reached during the 8th week of the study). This maximum once-daily dose was maintained through week 12. During week 13, the dose of the drug was decreased daily until participants were weaned from it.

All study participants also received twice-weekly, individual, cognitive-behavioral relapse prevention therapy. In cognitive-behavioral therapy, patients learn to confront the consequences of their drug use by recognizing the environmental cues and potentially stressful situations that trigger strong drug cravings, and develop avoidance strategies.

The scientists reported that participants who received topiramate were more likely than those who received a placebo to be cocaine-abstinent after the 8th week of the study. In addition, data from the 36 people who returned for at least one evaluation visit after starting medications showed that those who received topiramate and counseling were significantly more likely to achieve 3 or more weeks of continuous cocaine abstinence compared with those who received placebo and counseling (59 percent vs. 26 percent, respectively).

- **WHAT IT MEANS:** A recognized treatment for seizure disorders, topiramate also has been studied for treatment of alcoholism and opiate dependence. This study, however, is one of the first to explore its usefulness as a potential treatment for cocaine addiction. This study is important because it demonstrates that topiramate can successfully produce a stable period of cocaine abstinence. Previous research indicates that achieving a stable period of continuous cocaine abstinence is a predictor of long-term abstinence.

Dr. Kyle Kampman led this NIDA-funded study, which was published online in May, 2004 in *Drug and Alcohol Dependence*.

Cocaine Craving Activates Different Brain Regions in Women

New neuroimaging data show that cocaine-dependent women experience changes in regional cerebral blood flow that are different from the changes experienced by cocaine-dependent men. Cerebral blood flow is a correlate of neural activity in the brain.

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Dr. Clinton Kilts and his colleagues at Emory University School of Medicine in Atlanta used positron emission tomography (PET) to examine blood flow related to drug craving in the brains of 8 abstinent, cocaine-craving women; results were compared with samples from 8 matched cocaine-craving men who underwent the same process. Craving was provoked by mental imagery induced by a 1-minute narration describing past individual cocaine use. The scientists also assessed regional cerebral blood flow when the study participants listened to narrations of drug-neutral experiences.

The researchers found that cue-induced craving was associated with greater activation of the central sulcus and frontal cortex in women, and less activation of the amygdala, insula, orbitofrontal cortex, and ventral cingulated cortex. Both men and women demonstrated activation of the right nucleus accumbens. Perhaps most notable was the neural activity measured in the amygdalas of study subjects; the women experienced a marked decrease in activity, in contrast to the increase observed in men. The amygdala is involved in controlling social and sexual behavior and emotions. The other related areas of the brain are involved in emotion and cognition.

- **WHAT IT MEANS:** The differences noted in this study, coupled with the results of studies like this that more precisely define gender differences in drug abuse, may support the need to develop gender-specific strategies to treat drug abuse.

This NIDA-funded study was published in the February 2004 issue of the *American Journal of Psychiatry*.

Adolescent, Adult Rats Respond Differently to Nicotine and Nicotine-Related Environments

One critical aspect of drug addiction is the effect of conditioned cues on drug-seeking behavior. Scientists at the University of Wisconsin–Madison have reported that adolescent and adult rats exhibit different behaviors in response to nicotine and nicotine-related environments, suggesting there are molecular differences in adolescent and adult rat brains.

The researchers examined how injections of nicotine stimulated movement in rats. Over 10 days, the scientists injected nicotine or saline into 16 adolescent and 16 young adult male rats. Immediately following the injections, they placed the rats in plastic chambers and observed their movements for 90 minutes.

The stimulant properties of nicotine caused rats in both groups to walk or run more, but the drug had a greater overall effect on adults. It also significantly increased rearing (standing on hind legs), a sign of curiosity and exploring, in adults. But the scientists' key finding was that adolescent rats, when re-exposed to the plastic chamber following a saline injection, failed to show any enhanced motor activity in the absence of nicotine. The adult rats, on the other hand, did exhibit drug-induced cue conditioning as evidenced by increased movement in the drug-paired environment following a saline injection. The scientists speculate that the drug-associated conditioning seen in adult rats is associated with specific brain regions and circuitry that may not be mature in adolescent rats.

- **WHAT IT MEANS:** These findings are an important step toward understanding the biological effects of nicotine on the adolescent brain, and suggest that plasticity—the ability of the brain to form new connections between nerve cells, a process that occurs predominantly during youth—may be partly responsible for differences between adolescents and adults regarding drug-seeking behaviors. This study implies that the development of brain systems involved in drug abuse may begin in adolescence.

Lead author Terri Schochet and her colleagues published this NIDA-supported study in the online version of the April 2004 issue of *Psychopharmacology*.

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Upcoming Meetings

Great Lakes Blending Conference Scheduled

The Blending Conference—Blending Clinical Practice and Research: Forging Partnerships in the Great Lakes States to Enhance Drug Addiction Treatment—will take place September 27–28 at the Marriott Renaissance in Detroit.

The 2-day conference will bring together clinicians and researchers to examine cutting-edge scientific findings about drug abuse and addiction, and their applications to clinical practice. It is designed to bridge the gap that exists between scientific research and clinical practice.

NIDA and the Great Lakes Clinical Trials Network (CTN) Node at Wayne State University are among the meeting's many co-sponsors.

More details about the conference can be found on NIDA's Web site at www.drugabuse.gov.

For more information about any item in this *NewsScan*:

- **Reporters**, call **Michelle Person** at 301-443-6245.
- **Congressional staffers**, call **Mary Mayhew** at 301-443-6071.

The National Institute on Drug Abuse (NIDA) is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports more than 85 percent of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice. Fact sheets on the health effects of drugs of abuse and other topics are available in English and Spanish. These fact sheets and further information on NIDA research and other activities can be found on the NIDA home page at **http://www.drugabuse.gov**.

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